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Applicants : Adrian Gilbert et al. Examiner: A. DeCloux

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Assistant Commissioner for Patents
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SIR:

INFORMATION DISCLOSURE STATEMENT
PURSUANT TO 37 C.F.R. §1.97(b)(3)

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following Reference Items 1-164 **(Exhibits 1-154)** which are listed again on the accompanying Form PTO-1449 **(Exhibit A)**. Applicants request that the Examiner review the references and make them of record in the subject application.

This Information Disclosure Statement is being submitted before the issuance of a first Office Action on the merits in connection with the subject application. Accordingly, no fee is required and this Information Disclosure Statement shall be considered pursuant to 37 C.F.R. §1.97(b)(3).

For the convenience of the Examiner, applicants point out that Reference Items 8, 26, 28, 146-148, 156, 160-161, and 163 were cited in the May 24, 2001 International Search Report in the corresponding PCT International Application, and a copy of the Report is enclosed as **Exhibit B**.

Applicants also point out that several of the listed references are counterparts of each other and are cumulative. Therefore, in accordance with 37 C.F.R. § 1.98(c), a counterpart of a reference is identified after the cite to the reference, but a copy of only one of the counterparts is being provided. Applicants will provide the Examiner with copies of any reference upon request.

1. U.S. Patent No. 3,849,550, issued November 19, 1974 (Teitelbaum, et al.) **(Exhibit 1)**;

2. U.S. Patent No. 4,339,431, issued July 13, 1982 (Gaffar) **(Exhibit 2)**;

3. U.S. Patent No. 5,204,099, issued April 20, 1993 (Barbier, et al.) **(Exhibit 3)**;

4. U.S. Patent No. 5,591,629, issued January 7, 1997 (Rodriguez et al.) **(Exhibit 4)**;

5. U.S. Patent No. 5,627,206, issued May 6, 1997 (Hupe, et al.) **(Exhibit 5)**;

6. U.S. Patent No. 5,668,117, issued September 16, 1997 (Shapiro) **(Exhibit 6)**;

7. U.S. Patent No. 5,719,296, issued February 17, 1998 (Acton, III, et al.) **(Exhibit 7)**;

8. U.S. Patent No. 5,800,808, issued September 1, 1998 (Konfino,

et al.) **(Exhibit 8)**;

9. U.S. Patent No. 5,858,964, issued January 12, 1999 (Aharoni, et al.) **(Exhibit 9)**;

10. U.S. Patent No. 5,981,589, issued November 9, 1999 (Konfino, et al.) **(Exhibit 10)**;

11. U.S. Patent No. 5,958,972, issued September 28, 1999 (Hupe, et al.) **(Exhibit 11)**;

12. U.S. Patent No. 6,048,898, issued April 11, 2000 (Konfino, et al.) **(Exhibit 12)**;

13. U.S. Patent No. 6,054,430, issued April 25, 2000 (Konfino, et al.) **(Exhibit 13)**;

14. U.S. Patent No. 6,214,791, issued April 10, 2001 (Arnon, et al.) **(Exhibit 14)**;

15. U.S. Patent No. 6,342,476, issued January 29, 2002 (Konfino, et al.) **(Exhibit 15)**;

16. U.S. Serial No. 09/359,099, filed July 12, 1999 (Strominger et al.) **(Exhibit 16)**;

17. U.S. Serial No. 09/405,743, filed September 24, 1999 (Gad et al.) **(Exhibit 17)**;

18. U.S. Serial No. 09/768,872, filed January 23, 2001 (Aharoni et

al.) **(Exhibit 18)**;

19. U.S. Serial No. 09/816,989, filed March 23, 2001 (Gad et al.). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/405,743 (Exhibit 17);

20. U.S. Serial No. 09/875,429, filed June 5, 2001 (Yong and Chabot) **(Exhibit 19)**;

21. U.S. Serial No. 09/885,227, filed June 20, 2001 (Rodriguez and Ure) **(Exhibit 20)**;

22. PCT International Application No. PCT/US88/02139 (WO 88/10120), published December 29, 1988 (Weiner et al.) **(Exhibit 21)**;

23. PCT International Application No. PCT/US95/06551 (WO 95/31990), published November 30, 1995 (Konfino et al.). Applicants point out that this reference is a counterpart of U.S. Patents Nos. 5,800,808 (Exhibit 8) and 6,342,476 (Exhibit 15);

24. PCT International Application No. PCT/EP95/02125 (WO 95/33475), published December 14, 1995 (Kott et al.) **(Exhibit 22)**;

25. PCT International Application No. PCT/US98/00375 (WO 98/30227), published July 16, 1998 (Arnon et al.). Applicants point out that this reference is a counterpart of US Patent No. 6,214,791 (Exhibit 14);

26. PCT International Application No. PCT/US99/16747 (WO 00/05250), published February 3, 2000 (Aharoni et al.). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/768,872 (Exhibit 18);

27. PCT International Application No. PCT/US99/22402 (WO 00/18794), published April 6, 2000 (Gad et al.). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/405,743 (Exhibit 17) and U.S. Serial No. 09/816,989;

28. PCT International Application No. PCT/US99/22836 (WO 00/20010), published April 13, 2000 (Flechter et al.) **(Exhibit 23)**;

29. PCT International Application No. PCT/US99/27107 (WO 00/27417), published May 18, 2000 (Aharoni et al.) **(Exhibit 24)**;

30. PCT International Application No. PCT/US99/16617 (WO 00/05249) published February 3, 2000 (Strominger et al.). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/359,099 (Exhibit 16);

31. PCT International Application No. PCT/US01/05198 (WO 01/60392) published August 23, 2001 (Gilbert et al.). Applicants point out that this reference is a counterpart of the subject application;

32. PCT International Application No. PCT/US01/18248 (WO 01/93828) published December 13, 2001 (Yong and Chabot). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/875,429 (Exhibit 19);

33. PCT International Application No. PCT/US01/19649 (WO 01/97846) published December 27, 2001 (Rodriguez and Ure). Applicants point out that this reference is a counterpart of U.S. Serial No. 09/885,227 (Exhibit 20);

34. European Patent Application No. 0 383 620 A2, published August 22, 1990 (Cook) **(Exhibit 25)**;

35. European Patent No. 0 359 783 B1, published November 29, 1995 (Weiner, et al.). Applicants point out that this reference is a counterpart of PCT International Application No. PCT/US88/02139 (Exhibit 21);

36. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis by a Synthetic Polypeptide", Eur. J. Immunol., 1971, 1, 242-248 **(Exhibit 26)**;

37. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis by a Synthetic Polypeptide", Israel J. Med. Sci., 1971, 7, 630-631 (Abstract) **(Exhibit 27)**;

38. Arnon, et al., "Suppression of Experimental Allergic Encephalomyelitis by a Synthetic Copolymer Immunological Cross Reactive with Basic Encephalitogen", Israel J. Med. Sci., 1972, 8, 1759-1760 **(Exhibit 28)**;

39. Teitelbaum, et al., "Protection Against Experimental Allergic Encephalomyelitis", Nature, 1972, 240, 564-566 **(Exhibit 29)**;

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41. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis with Basic Polymers", Eur. J. Immunol., 1973, 3, 273-279 **(Exhibit 31)**;

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43. Teitelbaum, et al., "Dose-response Studies on Experimental Allergic Encephalomyelitis Suppression by COP-1", Israel J. Med. Sci., 1974, 10(9), 1172-1173 **(Exhibit 33)**;

44. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis in Rhesus Monkeys by a Synthetic Basic Copolymer", Clin. Immunol. Immunopath., 1974, 3, 256-262 **(Exhibit 34)**;

45. Webb, et al., "Suppression of Experimental Allergic Encephalomyelitis in Rhesus Monkeys by a Synthetic Basic Copolymer", Isr. J. Med. Sci., 1975, 11, 1388 (Abstract) **(Exhibit 35)**;

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47. Abramsky, et al., "Effect of a Synthetic Polypeptide (COP-1) on Patients with Multiple Sclerosis and with Acute Disseminated Encephalomyelitis", J. Neurol. Sci., 1977, 31, 433-438 **(Exhibit 37)**;

48. Teitelbaum, et al., "Suppression of Experimental Allergic Encephalomyelitis in Baboons by Cop 1", Israel J. Med. Sci., 1977, 13, 1038 (Abstract) **(Exhibit 38)**;

49. Arnon, et al., "Suppression of EAE in Baboons by a Synthetic Polymer of Amino Acids", Neurol., 1978, 28, 336 (Abstract) **(Exhibit 39)**;

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53. Lando, et al., "Effect of Cyclophosphamide on Suppressor Cell Activity in Mice Unresponsive to EAE", J. Immunol., 1979, 123, 2156-2160. (Abstract) **(Exhibit 43)**;

54. Lando, et al., "Experimental Allergic Encephalomyelitis in Mice - Suppression and Prevention with COP-1", Israel J. Med. Sci., 1979, 15, 868-869 (Abstract) **(Exhibit 44)**;

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59. Bornstein, et al., "Treatment of Multiple Sclerosis with a Synthetic Polypeptide: Preliminary Results", Ann. Neurol., 1980, 8, 117 (Abstract) **(Exhibit 49)**;

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Synthetic Polypeptide: Preliminary Results", Trans. Am. Neurol. Assoc., 1980, 105, 348-350 **(Exhibit 50)**;

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62. Arnon, "Experimental Allergic Encephalomyelitis - Susceptibility and Suppression", Immunological Rev., 1981, 55, 5-30 **(Exhibit 52)**;

63. Bornstein, et al., "Multiple Sclerosis: Trial of a Synthetic Polypeptide", Ann. Neurol., 1982, 11, 317-319 **(Exhibit 53)**;

64. Brosnan, et al., "The Response of Normal Human Lymphocytes to Copolymer 1", J. Neuropath. Exp. Neurol., 1983, 42, 356 (Abstract) **(Exhibit 54)**;

65. Lisak, et al., "Effect of Treatment with Copolymer 1 (Cop-1) on the in Vivo and in Vitro Manifestations of Experimental Allergic Encephalomyelitis (EAE)", J. Neurol. Sci., 1983, 62, 281-293 **(Exhibit 55)**;

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Sclerosis (MTP Press, The Hague, 1984) 144-150 **(Exhibit 57)**;

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71. Burns, et al., "Human Cellular Immune Response in Vitro to Copolymer 1 and Myelin Basic Protein (MBP)", Neurol., 1985, 35 (Suppl. 1), 170 (Abstract) **(Exhibit 61)**;

72. Teitelbaum, et al., "Monoclonal Antibodies to Myelin Basic Protein Cross React with Synthetic EAE-suppressive Copolymer, COP 1" in Proc. 7th Eur. Immunol. Mtg., Jerusalem, September 8-13, 1985 (Abstract) **(Exhibit 62)**;

73. Thompson, "MCQ Tutor: Medical Immunology Multiple Choice Questions", Immunol. Today, 1985, 6(4), 141 **(Exhibit 63)**;

74. Burns, et al., "Human Cellular Immune Response to Copolymer 1 and Myelin Basic Protein", Neurol., 1986, 36, 92-94 **(Exhibit 64)**;

75. Bornstein, "Cop 1 May be Beneficial for Patients with Exacerbating-remitting Form of Multiple Sclerosis", Adv. Ther. (USA), 1987, 4, 206 (Abstract) **(Exhibit 65)**;

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77. Rolak, "Copolymer-I Therapy for Multiple Sclerosis", Clin. Neuropharmacology, 1987, 10(5), 389-396 **(Exhibit 67)**;

78. Winer, "COP 1 Therapy for Multiple Sclerosis", New Eng. J. Med., 1987, 317(7), 442-444 **(Exhibit 68)**;

79. Arnon, et al., "Suppression of Demyelinating Diseases by Synthetic Copolymers", in A Multidisciplinary Approach to Myelin Disease (G. Serlupi Crescenzi, ed., Plenum Publishing Corp., 1988) 243-250 **(Exhibit 69)**;

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83. Arnon, et al., "Suppression of Experimental Allergic Encephalomyelitis by Cop-1 - Relevance to Multiple Sclerosis", Israel J. Med. Sci., 1989, 25, 686-689 **(Exhibit 73)**;

84. Bornstein, et al., "Pilot Trial of COP-1 in Chronic Progressive Multiple Sclerosis: Preliminary Report", from The International Multiple Sclerosis Conference: An Update on Multiple Sclerosis, Roma (Italy), September 15-17, 1988, in Elsevier Science Publisher, 1989, 225-232 **(Exhibit 74)**;

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87. Carter, et al., "Newer Drug Therapies for Multiple Sclerosis", Drug Therapy, 1990, 31-32, 37-39, 42-43 **(Exhibit 77)**;

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93. Starzl, Transplantation Proceedings, 1990, 22 (1, Suppl. 1), 5 **(Exhibit 83)**;

94. Wender, "Copolymer 1 (COP-1) in the Treatment of Multiple Sclerosis (letter)" Neur. Neurochir. Pol., 1990, 24, 113 **(Exhibit 84)**;

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96. Burns, et al., "Failure of Copolymer 1 to Inhibit the Human T-cell Response to Myelin Basic Protein", Neurol., 1991, 41, 1317-1319, **(Exhibit 86)**;

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98. Ferrara, et al., "Graft-Versus-Host Disease", New Eng. J. Med., 1991, 324, 667-674 **(Exhibit 88)**;

99. Meiner, "COP-1 Multicenter Clinical Trial in Exacerbating-remitting Multiple-Sclerosis: One Year Follow-up", J. Neurol., 1991(Suppl. 1) (Abstract) **(Exhibit 89)**;

100. Rothbard, et al., "Interactions Between Immunogenic Peptides and MHC Proteins", Ann. Rev. Immunol., 1991, 9, 527-565 **(Exhibit 90)**;

101. Salvetti, et al., "Myelin Basic Protein T Cell Epitopes in Patients with Multiple Sclerosis", Department of Neurological Sciences, University of Rome, La Sapienza 1991, 72 (Abstract) **(Exhibit 91)**;

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107. Racke, et al., "Copolymer-1-induced Inhibition of Antigen-specific T Cell Activation: Interference with Antigen Presentation", J. Neuroimmunol., 1992, 37, 75-84 **(Exhibit 97)**;

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109. Weinshenker, et al., "Natural History and Treatment of Multiple Sclerosis", Current Opinion in Neurol. and Neurosurgery, 1992, 5, 203-211 **(Exhibit 99)**;

110. Aharoni, et al., "T Suppressor Hybridomas and Interleukin-2-Dependent Lines Induced by Copolymer 1 or by Spinal Cord Homogenate Down-Regulate Experimental Allergic Encephalomyelitis", Eur. J. Immunol., 1993, 23, 17-25 **(Exhibit 100)**;

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115. Keleman, et al., "Graft-versus-Host Disease in Bone Marrow Transplantation: Experimental, Laboratory, and Clinical Contributions of the Last Few Years", Int. Arch. Allergy Immunol., 1993, 102, 309-320 **(Exhibit 105)**;

116. Gurevich, "Study of the MHC-competition Between BP and Cop 1 Using Human Cytotoxic T-cell Clones", Israel J. Med. Sci., 1993 (Abstract) **(Exhibit 106)**;

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119. Sela, "Polymeric Drugs as Immunomodulatory Vaccines Against Multiple Sclerosis", Makromol. Chem. Macromol. Symp., 1993, 70/71, 147-155 **(Exhibit 109)**;

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125. Fridkis-Hareli, et al., "Copolymer 1 Displaces MBP, PLP and MOG, but Can Not be Displaced by these Antigens from the MHC Class II Binding Site", Department of Chemical Immunology, The Weizmann Institute of Science, 1994 **(Exhibit 115)**;

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127. Fridkis-Hareli, et al., "Specific and Promiscuous Binding of Synthetic Copolymer 1 to Class II Major Histocompatibility Complex Molecules on Living Antigen Presenting Cells", Israeli Biochem. Soc., 1994, 21-22 (Abstract) **(Exhibit 117)**;

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137. Milo, et al., "Additive Effects of COP-1 and IFN-Beta on Immune Responses to Myelin Basic Protein", Neurol., 1994, 44(Suppl. 2), A212 **(Exhibit 127)**;

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Medical Center, Sackler School of Medicine, Tel-Aviv University of Maryland School of Medicine, 1994, 22 **(Exhibit 128)**;

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140. Nightingale, et al., "Access to Investigational Drugs for Treatment Purposes", Am. Family Physician, 1994, 50(4), 845-847 **(Exhibit 130)**;

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If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone at the number provided below.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby give to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231

7/2/02

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